TGFβ1/Affinity-bound Alginate Scaffold Enhances Chondrogenic Differentiation of Human Mesenchymal Stem Cells (hMSC)
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Introduction
MSC differentiation profile depends on the environment wherein cells reside, especially on the spatio-temporal presentation of differentiation-inductive growth factors. Herein, we aimed to reconstruct the microenvironment, which promotes chondrogenic differentiation, by presenting the chondro-inductive Transforming Growth Factor β1 (TGFβ1), in a similar manner to its presentation by the extra-cellular matrix. Thus, TGFβ1 was affinity-bound to alginate-sulfate containing scaffold, mimicking the specific interactions of this factor with heparan sulfate. 1

Materials and Methods
TGFβ1/affinity-bound to alginate-sulfate containing scaffolds were prepared by a freeze-dry technique (200ng protein/scaffold). The released TGFβ1 from the scaffolds was analyzed by ELISA, and its bioactivity by measuring collagen deposition in fibroblast culture. HMSC were seeded into TGFβ1/affinity-bound scaffolds (300,000 cells/scaffold), and TGFβ1-induced chondrogenic signal-transduction pathways were tested by Western Blot. Collagen deposition in hMSC constructs was detected by Masson's trichrome staining.

Results
In vitro release study showed the sustained release of TGFβ1 for 7 days from the affinity-binding alginate scaffolds, compared to the burst release of nearly 100% of the entrapped TGFβ1 from alginate scaffolds (p, interaction<0.0001, 2-way ANOVA). TGFβ1 retained its biological activity, as assessed by its ability to enhance collagen deposition in fibroblast culture. Prolonged expression of phosphorylated Smad2 and increased phosphorylation level of ERK1/2 for up to 14 days in hMSCs culture within TGFβ1/affinity-binding scaffolds, indicate the long-term activity of TGFβ1 in this system. Masson's trichrome staining of 14 day-old constructs demonstrated massive deposition of collagen in the TGFβ1/affinity-bound scaffolds.

Discussion and Conclusions
These data indicate the potential use of the affinity-binding alginate scaffolds combined with spatial presentation of TGFβ1 for reconstruction of the microenvironment for neo-cartilage formation.

References

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Disclosures
The authors have nothing to disclose.